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EXAMINER	
TRAN, SUSAN T	

ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/630,633	BREITENBACH ET AL.	
	Examiner	Art Unit	
	S. Tran	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,18 and 20-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,18 and 20-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-16, 18 and 20-25 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 28-59 of copending Application No. 10/523908 ('908). Although the conflicting claims are not identical, they are not patentably distinct from each other because application '908 claimed a transdermal therapeutic system (TTS) comprising a drug-containing hot-melt adhesive matrix produced by metering the drug into the solvent-free melt of the adhesive matrix at a temperature of 102°C-160°C. The TTS further comprises a drug and a softener (claims 28 and 31). Hot-melt adhesive includes amine-resistant silicone (claim 31). Softeners are found in claims 32 and 33. Drug include Rotigotine is found in

claims 28, 29 and 42-44. Amount of drug is found in claims 34-36. Drug present in form of a base is found in claim 37. Release profile is found in claims 46-48. Accordingly, the present claims are anticipated by the claims of the '908 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a TTS comprising hot-melt adhesive matrix and Rotigotine, does not reasonably provide enablement for the release profiles recite in claims 14 and 15. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (a)). These include: breadth of the claims, nature of the invention, state of the prior art, amount of direction provided by the inventor, the level of predictability in the art, the existence of working examples, quantity of experimentation needed to make or use the invention based on the content of the disclosure, and relative skill in the art. All of the

factors have been considered with regard to the claim, with the most relevant factors being discussed below:

Breadth of the Claims: is broad. Independent claim 14 is directed to a TTS of Rotigotine characterized in that for a period of at least 5 days following its application on human skin, the TTS induces in the patient an average plasma concentration of 0.4 to 2 ng per ml Rotigotine.

Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Claims 14-16 do not recite the structure of the TTS that contain any adhesive matrix and softener in the amounts that would result in the claimed release profiles.

Amount of direction provided by the inventor: the present specification discloses a specific TTS that exhibits the specific release profiles recite in the claims. See for example specification at pages 16-18, and examples. The TTS contains specific silicone-base hot-melt. The present specification, however, does not teach how to precisely achieve the claimed release profiles given any TTS using any type of materials in any amount. This is further impossible in view of the multitudes of types of suitable transdermal polymers such as water-soluble, water-insoluble, and etc. The specification also fails to teach if all of the claimed properties can be achieved with all type of transdermal polymers in any amount, and in any structures. The specification does not provide any guidance as to how one can achieve the claimed specific release profile with any type of dosage structures, such as single layer, non-adhesive layer,

multi-adhesive layer, pressure sensitive coating layer, and so on. Accordingly, a burdensome amount of research would be required by one of ordinary skill in the art to bridge this gap.

As such, the practitioner would turn to trial and error experimentation in order to compose a TTS comprising Rotigotine, without guidance from the specification or the prior art.

The relative skill of those in the art: the skill of those in the art is very high, *e.g.*, Ph.D. or M.D. level technology.

Claim 10 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. It appears that the specification does not provide support for the limitation "hydrophilic *and* amphiphilic polymers" and "hydrophilic *and* amphiphilic copolymers". It is noted that the present specification at page 15, discloses "hydrophilic **or** amphiphilic polymers" and "hydrophilic **or** amphiphilic copolymers".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

> invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-16, 18 and 20-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. US 5,807,570, in view of Metman et al. (Clinical Neuropharmacology) and Noel US Re. 36,754.

Chen teaches a TTS comprising a backing layer, and an adhesive polymeric matrix which contains combination of a permeation enhancer and at least about 30% ropinirole or an analog thereof as an active agent (abstract; column 3, lines 1-37; column 4, lines 25-37; and column 6, lines 36-46). Permeation enhancer includes polyethylene glycol, propylene glycol, alcohol, and the like (column 7, lines 24-39). Active agent can be administered in the form of a base or pharmaceutically acceptable salt (column 7, lines 6-10). The polymeric matrix further comprises pressure sensitive adhesive polymer including silicone (column 8, lines 48-67).

Chen does not expressly teach the claimed active agent.

Metman teaches transdermally administering rotigotine for the treatment of Parkinson's disease (abstract). Thus, it would have been obvious to one of ordinary skill in the art to modify the TTS of Chen to include rotigotine as an active agent in view of the teaching of Metman, because Metman teaches that rotigotine is an effective treatment for advanced Parkinson's disease with mild adverse effects compare to other active agent, because Metman teaches using rotigotine for the treatment of Parkinson's disease allows patients to substantially lower L-Dopa doses without loss of antiparkinsonian efficacy, and because Chen teaches the desirability to obtain a TTS useful for the treatment of Parkinson's disease.

Chen further does not teach the matrix system that comprises organic wax.

Noel teaches a hot-melt silicone-base TTS comprising silicone sensitive adhesive, and organic waxes having melting point between 30-150°C (abstract). Organic waxes include vegetable waxes, animal waxes, mineral waxes such as ozokerite, and mixtures thereof in an amount of from about 1 to about 25% (column 5, lines 1-11; and claim 17). Silicone sensitive adhesive is present in an amount from about 99-85% (column 8, lines 41-44). Noel further teaches the hot-melt silicone-base TTS is free of solvent (column 2, lines 66-67). Thus, it would have been obvious to one of ordinary skill in the art to modify the TTS of Chen using the hot-melt silicone-base TTS in view of the teaching of Noel to obtain the claimed invention. This is because Noel teaches a transdermal system that is highly efficacious, because Noel teaches using organic waxes to decrease viscosity and improve coatability which do not require the present of solvents (column 1, lines 66 through column 2, lines 1-3), because Noel teaches using organic waxes over the use of solvents to avoid: 1) removal and containment of solvents, 2) special precautions to avoid fires, and 3) cost effectiveness (ID), because Chen teaches a TTS that comprises silicone and waxes as carriers (column 6, lines 25-27), and because Chen teaches the desirability to obtain a TTS that improved patient compliance and with less side effects (column 2, lines 51-60).

Response to Arguments

Applicant's arguments filed 04/18/08 have been fully considered but they are not persuasive.

Applicant states that Applicant may elect to argue to overcome the provisional obviousness-type double patenting rejection or to provide a terminal disclaimer (to the extent necessary) once the present claims have been found to be otherwise allowable and/or once the co-pending application issues as a patent.

Accordingly, the rejection is maintained.

Applicant argues that by amendment herein, Claim 14 (and Claim 15 dependent thereon) is amended to depend from and incorporate the structural limitations of Claim 1. As the level of skill in the art is very high (as admitted in the present Action, page 5), one of skill in the art can without undue experimentation, using standard pharmacokinetic protocols, test any TTS failing within the scope of Claim 1 and determine whether it meets the functional limitations of Claims 14 and 15 (0.4-2 ng/ml average plasma concentration over a 5-day or 7-day period respectively). Furthermore, specific TTS's are described in the specification that meet these functional limitations; one of skill in the art can without undue experimentation prepare these TTS's and confirm the plasma levels attainable by their application, and can modify these TTS's and test the modified TTS's in order to determine whether they retain the plasma level properties shown.

However, in response to applicant's arguments, it is noted that claim 1 does not recite the structural that specifically allow one of ordinary skill in the art to make the invention without burdensome experimentation. Claim 1 is broad in the sense that it only recites the structure of the TTS. In order to achieve the claimed pharmacokinetic

profiles, a particular TTS with specific amounts, ratios, thickness and materials must be used. The examples in the present specification show only the use of hot melt silicon and one kind of softener, which is ozokerite. However, the present specification discloses that softener can be a wide variety of types including ozokerite, ceresine, paraffin, candelilla, carnauba, bee's wax, or mixtures of these waxes. Further the TTS requires the present of an internal phase components selected from a large group of polymers such as polysaccharides, substituted polysaccharides, polyethylene oxides, polyvinyl acetates, polyvinyl pyrrolidones (PVP), PVP with suitable softeners, polyethylene glycols, polypropylene glycols, acrylates, copolymers from PVP and (poly)vinyl acetate, copolymers from ethylene and vinyl acetate, and polyvinyl alcohols with a suitable softener such as glycerin. With all of this polymers to pick and chose, one of ordinary skill in the art have to go through a burdensome experimentation to select the compatible polymers, softener in any suitable amounts and/or ratios. This is further impossible in view of the multitudes of types of suitable transdermal polymers such as water-soluble, water-insoluble, and etc. The specification also fails to teach if all of the claimed properties can be achieved with all type of transdermal polymers in any amount, and in any structures. The specification does not provide any guidance as to how one can achieve the claimed specific release profile with any type of dosage structures, such as single layer, non-adhesive layer, multi-adhesive layer, pressure sensitive coating layer, and so on. Accordingly, a burdensome amount of research would be required by one of ordinary skill in the art to bridge this gap.

As such, the practitioner would turn to trial and error experimentation in order to compose a TTS comprising Rotigotine, without guidance from the specification or the prior art.

Accordingly, the 112, first paragraph rejection is maintained.

Applicant argues that one of ordinary skill could not have had reasonable expectation of success in preparing a TTS having rotigotine dispersed in a hot-melt adhesive, at least because rotigotine is sensitive to oxidation. In brief, one of ordinary skill would not have reasonably expected that use of a hot-melt process would be workable, due to sensitivity of rotigotine to oxidative decomposition. Furthermore, any influence of inclusion of organic wax in a hot-melt adhesive composition on release properties of rotigotine would not have been predictable to one of ordinary skill. In particular, it could not have been predicted that inclusion of a wax would not only provide rheological benefit in preparing the hot-melt TTS but would controllably retard release, making it possible to provide a TTS for administration over a period of 5-7 days. A surprising discovery showed that adding wax, especially organic wax such as ceresine or ozokerite, also has an effect on the *in-vitro* murine-skin permeation of rotigotine from the hot-melt silicone TTS. As is evident from FIG. 2, rotigotine's permeation rate decreases as the wax concentration increases ... This property of the wax is significant especially for developing a TTS designed for application over several days, for instance 7 days. That type of multi-day patch requires a high infusion of rotigotine, which poses the risk of an excessive release of rotigotine at the beginning of

the application phase ("dose dumping") ... Apart from the surprising discovery that the wax content in the matrix serves to retard the release of the active substance, varying the wax content will not only modify the dynamic viscosity of the adhesive but additionally offers the equally surprising option of regulating the active-substance release. The predictability of results required for a showing of obviousness under the KSR v. *Teleflex* standard is therefore absent.

However, in response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Chen teaches a similar TTS formulation to the claimed invention, which comprises active agent suitable for the treatment of Parkinson's disease. Although Chen teaches the use of waxes in the TTS, Chen does not teach organic waxes. However, the use of organic waxes in a TTS is well known in pharmaceutical art. See for example Noel et al. for the teachings of using organic wax in a TTS to ovoid using toxic organic solvents. The obtained TTS with the use of organic waxes is highly efficacious, and cost effectiveness. Chen is further combined with Metman for the teaching of the claimed active agent. Metman teaches rotigotine is a more effective active agent for the treatment of advanced Parkinson's disease, but offers very mild adverse effects

compare to other active agents. Therefore, one of ordinary skill in the art would have been motivated to modify the TTS of Chen to include rotigotine as an active agent.

Accordingly, the 103(a) rejection over Chen in view of Metman and Noel is maintained.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to S. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-F 8:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. Tran/
Primary Examiner, Art Unit 1618